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Airborne occupational exposures and risk of oesophageal and cardia adenocarcinoma

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Background: The reasons for the increasing incidence of and strong male predominance in patients with oesophageal and cardia adenocarcinoma remain unclear. The authors hypothesised that airborne occupational exposures in male dominated industries might contribute.

Methods: In a nationwide Swedish population based case control study, 189 and 262 cases of oesophageal and cardia adenocarcinoma respectively, 167 cases of oesophageal squamous cell carcinoma, and 820 frequency matched controls underwent personal interviews. Based on each study participant's lifetime occupational history the authors assessed cumulative airborne occupational exposure for 10 agents, analysed individually and combined, by a deterministic additive model including probability, frequency, and intensity. Furthermore, occupations and industries of longest duration were analysed. Relative risks were estimated by odds ratios (OR), with 95% confidence intervals (CI), using conditional logistic regression, adjusted for potential confounders.

Results: Tendencies of positive associations were found between high exposure to pesticides and risk of oesophageal (OR 2.3 (95% CI 0.9 to 5.7)) and cardia adenocarcinoma (OR 2.1 (95% CI 1.0 to 4.6)). Among workers highly exposed to particular agents, a tendency of an increased risk of oesophageal squamous cell carcinoma was found. There was a twofold increased risk of oesophageal squamous cell carcinoma among concrete and construction workers (OR 2.2 (95% CI 1.1 to 4.2)) and a nearly fourfold increased risk of cardia adenocarcinoma among workers within the motor vehicle industry (OR 3.9 (95% CI 1.5 to 10.4)). An increased risk of oesophageal squamous cell carcinoma (OR 3.9 (95% CI 1.2 to 12.5)), and a tendency of an increased risk of cardia adenocarcinoma (OR 2.8 (95% CI 0.9 to 8.5)), were identified among hotel and restaurant workers.

Conclusions: Specific airborne occupational exposures do not seem to be of major importance in the aetiology of oesophageal or cardia adenocarcinoma and are unlikely to contribute to the increasing incidence or the male predominance.

Two striking patterns of the epidemiology of oesophageal and gastric cardia adenocarcinoma in the Western world remain essentially unexplained: the increasing incidence[1–4] and the strong male predominance.[3 5 6] The sex distributions and the secular trends in prevalence of the established risk factors for these tumours—gastroesophageal reflux[7 8] and high body mass index (BMI)[9 10]—are not entirely consistent with these patterns. The rising incidence and the male predominance are more likely explained by as yet unidentified environmental exposures.[11] Several work related exposures may fulfil the criteria of affecting predominantly men and being introduced in the decades preceding the 1970s, before the increase in incidence seems to have started.[3] Few studies, however, have examined specific occupational exposures in relation to oesophageal or cardia adenocarcinoma. Therefore, we aimed to examine the importance of occupations and industries, with particular emphasis on specific airborne occupational exposures, especially in relation to risk of oesophageal and cardia adenocarcinoma, but also of oesophageal squamous cell carcinoma. We hypothesised that airborne chemicals or particles, occurring predominantly in male dominated industries, might be captured in the airways and swallowed to act as carcinogens directly on the oesophageal or cardia mucosa.

METHODS

Study design, data collection, and study participants

The design of this nationwide Swedish population based case control study has been described in detail previously.[8] The study included the entire native Swedish population of ages younger than 80 years and living in Sweden from 1995 through 1997. Eligible as cases were all newly diagnosed patients with oesophageal or gastric cardia adenocarcinoma and half of the patients with oesophageal squamous cell carcinoma (born on even numbered dates). A comprehensive organisation for case ascertainment, including contact people at all relevant hospital departments, ensured rapid identification of all eligible case patients. Controls were selected randomly from the Swedish register of the total population, and frequency matched according to the age and sex distribution of the cases of oesophageal adenocarcinoma. All tumours were uniformly documented and classified at surgery and endoscopy and one pathologist reviewed the histological slides. All study participants underwent computer aided personal interviews by professional interviewers. Informed consent was obtained from each study participant, and all regional ethics committees in Sweden approved the study.

Data on lifetime occupational history, occupations, and industries

The study questionnaire contained detailed information about lifetime occupational history, including questions about duration of employment, workplace, and work tasks for each occupation held by the study participant for at least one year. Each study participant's occupational history, ranging from 1–10 occupations, was coded by one reviewer (CJ), who was kept blinded for case/control status. We used the detailed, five digit Nordic Standard Occupational

Classification (NYK)[12] and the four digit Swedish Standard Industrial Classification (SNI).[13] Occupations held before 1955 were disregarded because they were considered to be outside the relevant aetiological time window. In the analyses we selected the study person's occupation or industry of longest duration (after 1955). These were aggregated into 66 occupational and 50 industry groups (two digit classifications). A given occupation or industry of longest duration (''exposed'') was compared to all the other occupations or industries of longest duration combined (''unexposed''; reference group).

Exposure assessment of airborne occupational exposures

We assessed cumulative occupational exposure for 10 airborne agents (wood dust, metal dust, asbestos, organic solvents, pesticides, diesel exhaust, quartz dust, flour dust, combustion gases, and unspecified dust). The assessments were done by a senior industrial hygienist (NP), based on manual reviews of each study participant's self reported occupational history, classified as described above. The reviewers (NP, CJ) had no information about case/control status. For the exposure assessment of wood dust, metal dust, asbestos, organic solvents, and pesticides we also used specific questions regarding number of yearly, monthly, or weekly regular contacts with these substances. The assessment of *cumulative exposure* to each substance was based on the following parameters: (a) *probability of exposure* on a scale of 0–2 (0 = no, 1 = possible, 2 = probable); (b) *frequency of exposure (part of week/year)* on a scale of 0–4 (0 = extremely small, 1 = very small, 2 = minor, 3 = medium, 4 = major); (c) *intensity of exposure*, considering different occupations and calendar periods, on a scale of 2–4 (2 = low, 3 = medium, 4 = high); and (d) *duration of exposure* (total number of exposed years for each relevant work period). The cumulative exposure score was calculated as the sum of (a) to (c) multiplied by (d).

Exposure assessment of diesel exhaust, quartz dust, flour dust, combustion gases, and unspecified dust (including, for example, oil mist, concrete dust, textile fibres, grinding dust, paper dust, aerosols, spray dust, frying fumes, soldering fumes) was based on the reviews of each study participant's occupational history and was measured as *duration of exposure* (total number of exposed years for each relevant work period). To analyse all airborne agents on the same scale we multiplied the duration of exposure by a weighted score of 6, corresponding to the midpoints of the scales of the parameters (that is, probability = 1, frequency = 2, and intensity = 3). The scores for cumulative exposure to quartz dust, flour dust, combustion gases, and unspecified dust were then summarised into one variable, labelled ''unspecified particular agents''.

The scores for cumulative exposure to wood dust, metal dust, asbestos, organic solvents, and pesticides were classified into three categories: no exposure (score = 0), low exposure, and high exposure. For low and high exposure the score was dichotomised according to the median among all exposed. The scores for cumulative exposure to diesel exhaust and unspecified particular agents were classified into four categories; no exposure (score = 0), low exposure, medium

Table 1 Occupational groups and risk of oesophageal and gastric cardia cancers

		Adenocarcinoma of oesophagus‡		Adenocarcinoma of gastric cardia‡		Squamous cell carcinoma of oesophagus‡	
Occupational group*†	Controls (n)	Cases (n)	OR§ (95% CI)	Cases (n)	OR§ (95% CI)	Cases (n)	OR¶ (95% CI)
Engineering and technical work	63	9	0.8 (0.4–1.8)	18	1.0 (0.6–1.8)	13	1.3 (0.7–2.7)
Educational work	39	4	0.4 (0.1–1.3)	9	0.8 (0.4–1.7)	2	0.2 (0.1–1.1)
Health service and nursing work	13	0	–	4	1.3 (0.4–4.4)	6	2.9 (1.0–8.8)
Social work	18	5	2.0 (0.6–6.8)	6	0.9 (0.3–2.6)	3	0.7 (0.2–2.6)
Government administrative work	11	0		1	0.3 (0.0–2.9)	1	0.7 (0.1–5.8)
Business administrative work	27	5	1.0 (0.3–3.2)	6	1.0 (0.4–2.5)	2	0.4 (0.1–2.0)
Accounting work	24	6	1.2 (0.4–3.3)	5	0.7 (0.3–1.9)	4	0.6 (0.2–2.2)
Secretarial and clerical work	19	3	0.8 (0.2–3.9)	5	0.9 (0.3–2.6)	7	1.6 (0.6–4.5)
Other administrative and clerical work	30	3	0.7 (0.2–2.4)	5	0.6 (0.2–1.6)	4	0.6 (0.2–2.0)
Buyers	11	0	–	2	0.6 (0.1–2.9)	0	–
Sales work	66	18	1.6 (0.9–3.0)	25	1.1 (0.7–1.9)	11	0.6 (0.3–1.3)
Agricultural, horticultural, and forestry management	52	17	1.1 (0.6–2.1)	18	1.1 (0.6–2.0)	4	0.7 (0.2–1.9)
Agriculture, horticultural, and livestock work	9	3	0.9 (0.2–4.2)	8	2.2 (0.8–6.0)	2	2.1 (0.4–10.7)
Forestry work	16	1	0.1 (0.0–1.2)	1	0.2 (0.0–1.3)	1	0.7 (0.1–5.6)
Road transport work	39	15	1.5 (0.7–3.0)	14	1.0 (0.5–1.9)	4	0.5 (0.2–1.4)
Engineering and building metal work	62	16	0.9 (0.4–1.7)	23	1.1 (0.6–1.9)	10	0.8 (0.4–1.8)
Electrical and electronic work	26	9	2.0 (0.8–5.1)	6	0.7 (0.3–1.9)	4	1.3 (0.4–4.1)
Wood work	13	1	0.1 (0.0–1.0)	7	1.7 (0.6–4.7)	4	2.7 (0.7–10.1)
Painting work	8	8	2.7 (0.9–8.6)	3	0.9 (0.2–3.4)	4	1.8 (0.5–7.0)
Concrete and other construction work	46	13	1.0 (0.5–2.1)	17	0.9 (0.5–1.7)	18	2.2 (1.1–4.2)
Printing work	8	2	3.6 (0.7–20.0)	1	0.7 (0.1–6.1)	0	–
Food and tobacco processing work	9	5	1.9 (0.5–7.4)	2	0.7 (0.1–3.7)	3	5.1 (1.2–21.0)
Pulp and paper work	7	2	1.1 (0.2–7.3)	1	0.5 (0.1–4.2)	1	1.3 (0.2–11.6)
Operation monitoring and material handling work	24	3	0.3 (0.1–1.1)	10	1.0 (0.4–2.1)	2	0.3 (0.1–1.6)
Hotel and restaurant work	8	2	1.2 (0.2–8.9)	7	2.8 (0.9–8.5)	7	3.9 (1.2–12.5)
Caretaking and cleaning work	13	5	2.3 (0.7–7.2)	4	0.9 (0.3–3.1)	3	0.7 (0.2–2.7)
Military work	8	0	–	4	1.8 (0.5–6.4)	1	0.4 (0.0–3.6)

*The total number of occupational groups (two digit occupational classifications) was 66. In the table we only present results from analyses of occupational groups including at least eight exposed control participants.
†In the analyses a given occupation of longest duration (''exposed'') was compared to all the other occupations of longest duration combined (''unexposed''; reference group).
‡Observations with missing data on any covariate included in the models were excluded from the analyses. There were eight oesophageal adenocarcinoma cases, six cardia adenocarcinoma cases, seven oesophageal squamous cell carcinoma cases, and 17 control participants with missing data on occupation. Four controls had missing data on BMI and were not included in the analyses of the adenocarcinomas.
§OR controlled for age and sex by matching and adjusted for reflux symptoms, BMI, and tobacco smoking.
¶OR controlled for age and sex by matching and adjusted for tobacco smoking and alcohol use.

Table 2 Industry groups and risk of oesophageal and gastric cardia cancers

		Adenocarcinoma of oesophagus‡		Adenocarcinoma of gastric cardia‡		Squamous cell carcinoma of oesophagus‡	
Industry group*†	Controls (n)	Cases (n)	OR§ (95% CI)	Cases (n)	OR§ (95% CI)	Cases (n)	OR¶ (95% CI)
Agriculture and hunting	51	20	1.4 (0.8–2.7)	18	1.1 (0.6–2.1)	4	0.7 (0.2–2.1)
Forestry	21	4	0.4 (0.1–1.4)	4	0.5 (0.2–1.4)	1	0.5 (0.1–3.8)
Food product and beverage industry	19	4	0.7 (0.2–2.4)	8	1.2 (0.5–2.9)	2	0.6 (0.1–2.9)
Wood production	12	3	0.4 (0.1–1.8)	5	1.0 (0.3–3.2)	2	1.6 (0.3–8.4)
Pulp and paper production	17	4	0.8 (0.2–2.7)	3	0.4 (0.1–1.4)	1	0.3 (0.0–2.9)
Publishers and printing industry	15	4	2.7 (0.7–9.7)	3	0.7 (0.2–2.5)	2	0.6 (0.1–3.4)
Chemical production	10	2	1.6 (0.3–8.7)	2	0.7 (0.1–3.3)	1	0.4 (0.0–3.5)
Non-metallic mineral production	8	1	0.5 (0.0–4.7)	4	1.5 (0.4–5.4)	3	2.3 (0.5–10.1)
Steel and metal production	12	2	0.9 (0.2–4.7)	2	0.6 (0.1–2.8)	1	0.8 (0.1–6.4)
Metal product industry	26	3	0.3 (0.1–1.0)	5	0.4 (0.2–1.2)	2	0.4 (0.1–2.0)
Machine production	20	9	1.2 (0.5–3.2)	5	0.8 (0.3–2.3)	3	1.0 (0.2–3.7)
Office machine and computer production	3	0	–	3	3.7 (0.7–21.1)	1	1.6 (0.1–21.1)
Tele product industry	13	3	1.6 (0.4–6.7)	2	0.6 (0.1–2.7)	2	0.9 (0.2–4.7)
Motor vehicle industry	10	3	1.3 (0.3–6.4)	10	3.9 (1.5–10.4)	2	1.3 (0.2–7.3)
Other transport equipment production	13	3	1.6 (0.4–7.0)	6	1.9 (0.6–5.4)	2	1.3 (0.3–6.4)
Furniture and other production	11	1	0.7 (0.1–5.7)	2	0.6 (0.1–2.8)	2	1.0 (0.2–5.3)
Electric power, gas, heat, and water	10	1	0.7 (0.1–6.3)	2	0.6 (0.1–2.9)	1	0.5 (0.1–4.5)
Construction industry	72	26	1.4 (0.8–2.4)	21	0.7 (0.4–1.2)	24	1.6 (0.9–2.8)
Motor vehicle trade and repair, petrol stations	18	9	2.2 (0.8–5.7)	10	1.5 (0.7–3.5)	5	1.2 (0.4–3.8)
Wholesale trade	27	5	1.1 (0.4–3.2)	6	0.7 (0.3–1.8)	1	0.3 (0.0–2.0)
Retail trade and repair shops	51	6	0.7 (0.3–1.7)	20	1.2 (0.7–2.2)	17	1.4 (0.7–2.6)
Hotels and restaurants	6	3	2.0 (0.3–11.3)	6	2.8 (0.8–9.3)	7	4.9 (1.4–17.3)
Land transport companies	51	14	1.2 (0.6–2.4)	19	1.0 (0.6–1.8)	6	0.5 (0.2–1.3)
Transport support and travel agencies	11	2	0.9 (0.2–4.9)	3	0.7 (0.2–2.6)	2	0.5 (0.1–2.5)
Post and telecommunications	12	2	0.7 (0.1–4.2)	4	1.1 (0.3–3.8)	4	1.2 (0.3–4.8)
Banks and other financial institutions	12	0	–	2	0.7 (0.1–3.5)	1	0.7 (0.1–5.6)
Insurance companies	6	2	2.5 (0.4–16.3)	1	0.5 (0.1–4.3)	0	–
Real estate companies	10	3	1.1 (0.3–4.9)	4	1.4 (0.4–4.9)	4	2.0 (0.5–7.2)
Other business service companies	24	2	0.7 (0.2–3.4)	5	0.9 (0.3–2.4)	6	1.1 (0.4–3.3)
Public sector and defence	68	14	1.3 (0.7–2.6)	23	1.2 (0.7–2.1)	12	0.8 (0.4–1.7)
Educational establishments	40	4	0.4 (0.1–1.2)	10	0.9 (0.4–1.8)	2	0.2 (0.1–0.9)
Health, nursing, and social services	50	6	0.8 (0.3–2.2)	12	0.9 (0.4–1.8)	14	1.3 (0.6–2.8)
Non-governmental and religious organisations	14	2	0.5 (0.1–3.1)	4	0.9 (0.3–3.1)	1	0.4 (0.0–3.4)
Recreational, cultural, and sporting establishments	7	0	–	3	1.4 (0.3–6.1)	2	1.1 (0.2–6.1)
Other personal services	6	1	0.6 (0.1–6.1)	1	0.6 (0.1–5.1)	1	0.9 (0.1–10.1)
Employment in households	5	3	1.2 (0.2–7.1)	1	0.5 (0.1–4.5)	4	1.8 (0.4–7.9)

*The total number of industry groups (two digit industrial classifications) was 50. In the table we only present results from analyses of industry groups including at least five exposed control participants.
†In the analyses a given industry of longest duration (''exposed'') was compared to all the other industries of longest duration combined (''unexposed''; reference group).
‡Observations with missing data on any covariate included in the models were excluded from the analyses. There were 10 oesophageal adenocarcinoma cases, eight cardia adenocarcinoma cases, nine oesophageal squamous cell carcinoma cases, and 24 control participants with missing data on industry. Four controls had missing data on BMI and were not included in the analyses of the adenocarcinomas.
§OR controlled for age and sex by matching and adjusted for reflux symptoms, BMI and tobacco smoking.
¶OR controlled for age and sex by matching and adjusted for tobacco smoking and alcohol use.

exposure, and high exposure. For low, medium, and high exposure the score was categorised according to the tertiles among all exposed.

Finally, to address the hypothesis that combined exposure to many airborne agents might exert a local, possibly mechanical effect on the oesophageal mucosa—independent of the specific exposure of each individual agent—we estimated the total exposure of particular agents. Cumulative exposure to wood dust, metal dust, asbestos, diesel exhaust, quartz dust, flour dust, combustion gases, and unspecified dust was summarised into one variable, by adding the scores into a total score. This variable, labelled ''total exposure of particular agents'', was classified into five categories; no exposure (total score = 0), low exposure, medium exposure, high exposure, and very high exposure. Low and medium exposure corresponded each to about 33% of all the exposed study participants, high exposure corresponded to 23% of all exposed, while very high exposure corresponded to 10% of all exposed. The cut offs were chosen as tertiles, where the upper tertile was subdivided to get an extreme group with very high exposure.

Statistical analyses

To estimate relative risks we used odds ratios (OR) and 95% confidence intervals (CI) estimated from conditional logistic regression,[14] using the PHREG procedure in SAS.[15] The regression models were conditional on the matching variables age and sex. In multivariable models, we adjusted for a priori known risk factors for the three different cancer types. Hence, in the analyses of oesophageal and cardia adenocarcinoma adjustments were made for reflux symptoms (heartburn and/or regurgitation at least 50 times/year, during at least one year of a study person's life, yes/no), BMI (kg/m^2, in four categories based on quartiles among the controls, 20 years before interview), and tobacco smoking status (in three categories—never, previous, current—two years before interview). In the analyses of oesophageal squamous cell carcinoma, adjustments were made for tobacco smoking status (categorised as above) and alcohol use (in four categories; 0, 1–15, 16–70, >70 grams per week, 20 years before interview). The influence of dietary intake of fruit and vegetables (in three categories of total intake, 20 years before interview) was evaluated, but as this variable did not change

Table 3 Airborne occupational exposures and risk of oesophageal and gastric cardia cancers

Airborne occupational exposure	Controls (n)	Adenocarcinoma of oesophagus* Cases (n)	OR† (95% CI)	p Value‡	Adenocarcinoma of gastric cardia* Cases (n)	OR† (95% CI)	p Value‡	Squamous cell carcinoma of oesophagus* Cases (n)	OR§ (95% CI)	p Value‡
Wood dust										
No exposure	732	166	1.0 (reference)		233	1.0 (reference)		149	1.0 (reference)	
Low exposure	35	7	0.8 (0.3–2.0)		12	1.1 (0.5–2.2)		2	0.4 (0.1–1.9)	
High exposure	32	8	0.6 (0.2–1.5)	0.50	11	1.0 (0.5–2.2)	0.97	9	2.0 (0.9–4.8)	0.13
Metal dust										
No exposure	744	175	1.0 (reference)		239	1.0 (reference)		151	1.0 (reference)	
Low exposure	29	2	0.1 (0.0–0.7)		6	0.5 (0.2–1.3)		5	1.1 (0.4–3.1)	
High exposure	26	4	0.4 (0.1–1.3)	0.02	11	1.4 (0.6–2.9)	0.24	4	1.2 (0.4–3.9)	0.92
Asbestos										
No exposure	692	154	1.0 (reference)		219	1.0 (reference)		141	1.0 (reference)	
Low exposure	56	13	0.9 (0.4–1.8)		16	0.7 (0.4–1.4)		10	0.9 (0.4–1.8)	
High exposure	51	14	0.9 (0.4–1.9)	0.92	21	1.2 (0.7–2.0)	0.52	9	0.9 (0.4–1.9)	0.88
Organic solvents										
No exposure	664	145	1.0 (reference)		218	1.0 (reference)		128	1.0 (reference)	
Low exposure	66	15	0.7 (0.4–1.5)		18	0.7 (0.4–1.3)		14	1.2 (0.6–2.3)	
High exposure	69	21	1.3 (0.7–2.3)	0.47	20	0.8 (0.5–1.4)	0.44	18	1.4 (0.7–2.5)	0.59
Pesticides										
No exposure	753	166	1.0 (reference)		236	1.0 (reference)		157	1.0 (reference)	
Low exposure	27	5	0.8 (0.3–2.3)		7	0.7 (0.3–1.8)		3	0.8 (0.2–3.0)	
High exposure	19	10	2.3 (0.9–5.7)	0.18	13	2.1 (1.0–4.6)	0.11	0	–	0.77
Diesel exhaust										
No exposure	700	156	1.0 (reference)		220	1.0 (reference)		142	1.0 (reference)	
Low exposure	34	7	0.7 (0.3–1.9)		9	0.5 (0.2–1.2)		10	1.7 (0.7–3.8)	
Medium exposure	34	6	0.7 (0.2–1.8)		12	0.9 (0.4–1.9)		6	0.8 (0.3–2.2)	
High exposure	31	12	1.1 (0.5–2.5)	0.74	15	1.2 (0.6–2.4)	0.43	2	0.4 (0.1–1.7)	0.33
''Unspecified particular agents''¶										
No exposure	471	79	1.0 (reference)		139	1.0 (reference)		90	1.0 (reference)	
Low exposure	114	37	1.4 (0.8–2.3)		34	0.7 (0.5–1.2)		17	1.0 (0.5–1.8)	
Medium exposure	111	27	1.0 (0.6–1.7)		43	1.1 (0.7–1.6)		26	1.7 (0.9–2.9)	
High exposure	103	38	1.3 (0.7–2.1)	0.52	40	1.1 (0.7–1.7)	0.50	27	1.7 (1.0–2.9)	0.14
''Total exposure of particular agents''**										
No exposure	363	60	1.0 (reference)		107	1.0 (reference)		72	1.0 (reference)	
Low exposure	158	35	1.0 (0.6–1.7)		43	0.7 (0.5–1.1)		27	1.1 (0.6–1.9)	
Medium exposure	145	41	0.9 (0.5–1.6)		45	0.8 (0.5–1.2)		34	1.7 (1.0–2.9)	
High exposure	95	39	1.3 (0.7–2.3)		40	1.1 (0.7–1.8)		19	1.4 (0.7–2.6)	
Very high exposure	38	6	0.4 (0.2–1.2)	0.37	21	1.6 (0.9–2.9)	0.11	8	1.8 (0.7–4.4)	0.29

*Observations with missing data on any covariate included in the models were excluded from the analyses. There were eight oesophageal adenocarcinoma cases, six cardia adenocarcinoma cases, seven oesophageal squamous cell carcinoma cases and 17 control participants with missing data on occupational history. Four controls had missing data on BMI and were not included in the analyses of the adenocarcinomas.
†OR controlled for age and sex by matching and adjusted for reflux symptoms, BMI and tobacco smoking.
‡Wald test of overall effect across all exposure strata.
§OR controlled for age and sex by matching and adjusted for tobacco smoking and alcohol use.
¶Cumulative exposure for quartz dust, flour dust, unspecified dust and combustion gases added.
**Cumulative exposure for wood dust, metal dust, asbestos and unspecified particular agents added.

the relative risk estimates for the exposures under study it was not included in the final models. Each exposure was evaluated using the Wald test, which considers all categories of the variable and not just pairwise comparisons to the reference category. Participants with missing data on any covariate included in the models were excluded from the analyses. Missing data were few, however, and fairly similar among case and control participants (tables 1–3).

RESULTS

Participation rates and characteristics of the study participants

The study included 189 oesophageal adenocarcinoma patients, 262 cardia adenocarcinoma patients, and 167 oesophageal squamous cell carcinoma patients, constituting 88%, 84%, and 73% respectively, of all eligible cases occurring in the study base. The 820 controls constituted 73% of all who were selected. The majority of the participants were men aged 60–79 years, and due to the matching there were no major differences regarding age or sex among non-participants and participants. Moreover, among 24 controls who initially declined to participate but later changed their minds (a group that could be regarded as a sample of the non-participating controls), the distribution of the known risk factors was similar to the other control persons (data not shown). General characteristics of the study participants have been described in detail previously.[16] After exclusion of 38 study participants due to missing or insufficient information regarding occupational history (tables 1–3), 1400 study participants remained. The mean length of the occupation of longest duration among the study participants was 24 years. Among the controls 55% had ever been exposed to particular agents (''total exposure of particular agents''), while the corresponding percentages among the patients with oesophageal adenocarcinoma, cardia adenocarcinoma, and oesophageal squamous cell carcinoma were 67%, 58%, and 55%, respectively.

Occupation and risk of oesophageal and gastric cardia cancers

In the multivariable models, we found no statistically significant associations between occupation of longest duration and risk of oesophageal adenocarcinoma. Non-significant excesses were found for sales work and painting work (table 1). Similarly, there were no statistically significant associations between occupation and risk of

cardia adenocarcinoma. A non-significantly increased risk was observed among hotel and restaurant workers (table 1). A twofold increased risk of oesophageal squamous cell carcinoma was identified among concrete and other construction workers (OR 2.2 (95% CI 1.1 to 4.2)). Positive associations were also seen between health service and nursing work (OR 2.9 (95% CI 1.0 to 8.8)), food and tobacco processing work (OR 5.1 (95% CI 1.2 to 21.0)) and hotel and restaurant work (OR 3.9 (95% CI 1.2 to 12.5)) and the risk of oesophageal squamous cell carcinoma, although the number of exposed cases were low (table 1).

Industry and risk of oesophageal and gastric cardia cancers

No statistically significant associations were identified between employment of longest duration in any specific industry and risk of oesophageal adenocarcinoma, except for a seemingly inverse association, based on three exposed cases only, between employment in the metal product industry and risk of this cancer (OR 0.3 (95% CI 0.1 to 0.9)) (table 2). We identified a nearly fourfold increased risk of cardia adenocarcinoma among people in the motor vehicle industry (OR 3.9 (95% CI 1.5 to 10.4)). A non-significantly increased risk of cardia adenocarcinoma (OR 2.8 (95% CI 0.8 to 9.3)) and a significantly increased risk of oesophageal squamous cell carcinoma (OR 4.9 (95% CI 1.4 to 17.3)) were found among people working in hotels or restaurants (table 2). A non-significantly increased risk of oesophageal squamous cell carcinoma was observed among those in the construction industry (OR 1.6 (95% CI 0.9 to 2.8)) (table 2).

Airborne occupational exposures and risk of oesophageal and gastric cardia cancers

A statistically significant inverse association, based on two exposed cases only, was observed between low metal dust exposure and risk of oesophageal adenocarcinoma (OR 0.1 (95% CI 0.0 to 0.7)) (table 3). We found statistically non-significant positive associations between high exposure to pesticides and risk of both oesophageal (OR 2.3 (95% CI 0.9 to 5.7)) and cardia adenocarcinoma (OR 2.1 (95% CI 1.0 to 4.6)) (table 3). Similarly, a tendency of a positive association was seen between high wood dust exposure and risk of oesophageal squamous cell carcinoma (table 3). Among workers highly exposed to ''unspecified particular agents'' a tendency of an increased risk of this tumour was found, compared to the unexposed (OR 1.7 (95% CI 1.0 to 2.9)) (table 3). No other statistically significant associations were found between airborne occupational exposures and risk of oesophageal or gastric cardia cancers (table 3).

DISCUSSION

This study revealed no major influence of airborne occupational exposures in the aetiology of oesophageal or cardia adenocarcinoma. There were indications of increased risks of both oesophageal and cardia adenocarcinoma among people highly exposed to pesticides, however. We found, unexpectedly, an increased risk of cardia adenocarcinoma among workers within the motor vehicle industry, but not of oesophageal adenocarcinoma. Oesophageal squamous cell carcinoma seemed to be more closely linked to occupational factors, where increased risks were observed among concrete and construction workers, hotel and restaurant workers, food and tobacco processing workers, and among people with health service and nursing work. Moreover, our data suggested that a high total number of inhaled particles may increase the risk of this tumour.

Strengths of this study include the population based design with a well defined study base, strict random sampling of controls, rapid and complete case ascertainment, and prospective and uniform tumour classification. Moreover, personal interviews with all study participants ensured high exposure information quality, and made it possible to adjust for all established risk factors. Despite our recruitment of almost all eligible patients throughout Sweden during a three year period, and although the exposure prevalence of combined particular agents was high (50–67%), the low incidence of these tumours and the low exposure prevalence to individual airborne agents, entailing limited power to detect even fairly strong associations, are weaknesses of our study. Furthermore, multiple testing could have generated some positive findings purely by chance. Moreover, recall bias is difficult to exclude. A limitation in studies examining occupational and industry groups is that these groups are only crude surrogates for specific occupational exposures, and variations within occupations are not considered, and an important strength of our study is the availability of detailed airborne occupational exposure data. However, the retrospective exposure assessment limited our ability to consider variations in the exposure levels that were not reflected in the self reported occupational history. The expert rating method employed—that is, expert raters reviewing occupational histories and allocating exposures—is however considered the best available tool for retrospective occupational exposure measurement.[17 18] Since 1955 is at least 40 years before diagnosis in our study, we considered any exposure before 1955 as less relevant. This is, however, an assumption with some uncertainty.

Our overall finding of a minor role of workplace exposures in the aetiology of oesophageal or cardia adenocarcinoma is consistent with one previous study examining occupational and industry groups, but not specific exposures, in relation to these tumours.[19] We were, however, unable to confirm the finding in this study of moderately increased risks of oesophageal adenocarcinoma among people employed in administrative support, health services, and financial, insurance, and real estate services, or the moderately increased risks of cardia adenocarcinoma among transportation or woodworking workers. Conversely, their results did not support our positive findings among occupational or industry groups.

The finding of possible positive associations between high exposure to pesticides and risk of oesophageal and cardia adenocarcinoma has not been reported before. In a study of agricultural pesticide use and risk of oesophageal and gastric adenocarcinomas, no significant associations were found,[20] and in another study of agricultural pesticide users, the mortality rates for oesophageal cancer were lower compared with the general population.[21] However, an increased risk of oesophageal cancer in areas with intensive farming[22] and a higher mortality of oesophageal cancer among agricultural workers engaged in intensive pesticide use[23] have been suggested. In our study, no significant associations between agricultural work and risk of oesophageal or cardia adenocarcinoma were identified, but our assessment of each study participant's individual pesticide exposure included all occupational exposure to pesticides, not only agricultural work. Moreover, about half of the agricultural workers in our study did not report any use of pesticides and were therefore considered unexposed, confirming the relatively low use of pesticides among farmers in Sweden. Our results might be explained by a threshold effect, with only a minority of workers exposed to pesticides exceeding this threshold. However, as the exposure prevalence among the cases was no more than 6%, the proportion of all cases occurring in the Swedish population that would be attributable to pesticides, if truly and causally linked to these tumours, would be small. Furthermore, we did not have detailed information about each person's individual working habits, and could therefore

Main messages

- Based on interviews, airborne occupational exposures were assessed on an individual level in a nationwide population based case control study, including 189 oesophageal adenocarcinoma patients, 262 cardia adenocarcinoma patients, 167 oesophageal squamous cell carcinoma patients, and 820 controls. Airborne occupational exposures do not seem to be of major importance in the aetiology of oesophageal or cardia adenocarcinoma.
- There were indications of increased risks of oesophageal and cardia adenocarcinoma among people highly exposed to pesticides.
- Increased risks of oesophageal squamous cell carcinoma were seen among concrete and construction workers and among people highly exposed to inhaled particles.

Policy implications

- In spite of the proportionately low handling of pesticides in Sweden, we observed indications of an excess risk. Additional research in studies where high frequency of pesticide activity occurs should explore in more detail the relation between exposure to pesticides and the risk of oesophageal and cardia adenocarcinoma.

not consider type of pesticide (product). Until more studies are conducted our findings need to be interpreted cautiously.

The increased risk of cardia adenocarcinoma among people employed in the motor vehicle industry cannot be explained by any specific airborne exposure, because the exposure pattern within this industry is heterogeneous.

The finding of increased risks of oesophageal squamous cell carcinoma among concrete and other construction workers and among those with high exposure of particular agents, including concrete dust, might be explained by our hypothesis of particles being captured in the airways, swallowed, and acting directly on the oesophageal mucosa. Previous studies have reported similar findings, where occupational exposure to silica dust and other dusts[24] and occupations potentially associated with exposure to silica dust, such as construction workers,[25] have been linked to oesophageal squamous cell carcinoma.

The increased risks of oesophageal squamous cell carcinoma and cardia adenocarcinoma among hotel and restaurant workers might be due to residual confounding by smoking or alcohol consumption. Other explanations include exposure to frying fumes or passive smoking. It is well known that exposure to environmental tobacco smoke is high among workers in restaurants and bars.[26]

In conclusion, airborne occupational exposures do not seem to be of major importance in the aetiology of oesophageal or cardia adenocarcinoma. Therefore, these exposures are unlikely to have contributed importantly to the increasing incidence or the male predominance of these tumours.

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